compression of the nerve root; the anterior tibial muscles are most frequently affected. Probably the commonest single finding is a decrease in, or the absence of the Achilles reflex on the affected side. Sensory disturbances of varying degree may be found in the thigh or leg, depending upon the nerve roots involved. The most frequent site is that referable to the fifth lumbar root, including the outer aspect of the leg and a portion of the dorsum of the foot.

X-RAY STUDIES

Plain x-ray films seldom add much to the diagnosis, except occasionally to show a decrease in the space between intervertebral disks; this may occur, however, without clinical signs of herniation. The final diagnosis must be made by spinal puncture and subsequent studies. Occasionally, the Queckenstedt test will show evidence of a partial or complete obstruction in the canal; but in the great majority the spinal fluid hydrodynamics are normal. The total protein content of the spinal fluid is often elevated above 50 milligrams per 100 cubic centimeters of spinal fluid in patients with ruptured intervertebral disks, but this finding is not sufficiently constant to depend upon. Lipiodol studies are essential to determine accurately the presence or absence of any encroachment on the dural sac. These studies are made on the fluoroscopic table, following the injection of from 3½ to 4 cubic centimeters of lipiodol. The patient is examined in the prone position on a tipping table, and any suspicious defect is immediately checked by x-ray films taken with the patient still on the fluoroscopic table. The deformity demonstrated varies from a complete block to the mere absence of one of the nerve-root cuffs, depending upon the size and location of the herniated disk. Lipiodol is not to be used indiscriminately, and we do not feel that it should be injected until a thorough trial of orthopedic measures of treatment has been given. Injection of the oil is often followed by a temporary increase in painful symptoms, though we have seen no permanent alterations which could be attributed to its use. Recently, the injection of air into the spinal canal has been advocated as a substitute for lipiodol in diagnosing deformities in the spinal canal. In 1934 Coggeshall and von Storch, and Van Wagenen described its use; and more recently Young and Scott reported a series of cases in which the diagnosis was made by the use of intraspinal air. Unfortunately, the contrast between air and the shadows cast by bone is not sufficient to outline accurately the smaller defects which often occur in herniations of the intervertebral disks. Consequently, one would hesitate to do a laminectomy on the basis of air studies alone, unless a large defect or block could be demonstrated. On the other hand, we should not feel safe in accepting a negative diagnosis when we know that many of the defects are so slight that they require careful study even with a good contrast shadow such as lipiodol produces. With the technique available at this time, I do not feel that we can fully rely upon intraspinal air studies to determine small deformities in the spinal canal.

DIAGNOSTIC PROBLEMS

Enlargement of the ligamentum flavum, a normal structure lying in the dorsal and lateral aspects of the spinal canal, may produce symptoms and findings identical with those of the herniated intervertebral disk. Even the studies with lipiodol may not differentiate between the two conditions. Such enlargements apparently result from rupture of the elastic fibers of the ligament, the subsequent formation of scar tissue and an increase in the size of the ligament.

TREATMENT

Laminectomy is required for either condition, with removal of the herniated disk or enlarged ligament. In some cases, protrusions of the disk may be removed extradurally if they lie in a lateral position, or transdurally if their location is more central. In most instances the damaged disk may be removed easily in one piece after the overlying ligamentous capsule has been incised. A few are firmly attached and require excision while, occasionally, the disk may be ossified so that removal is impossible. In such an instance the decompression of the nerve root will serve to relieve the symptoms.

If it is necessary to remove one or more facets, it is wise to follow the laminectomy immediately by spinal fusion to insure the stability of the back. This is particularly true in those patients who are accustomed to performing heavy work as a means of livelihood. In general, the patients who did not require fusion have been up and about in two or three weeks after operation, while those who have had bone grafts have remained in bed for from six to ten weeks.

The results of operation have been most satisfactory in the majority of patients. Pain has been relieved immediately, indicating that compression of the nerve was its cause. Improvement in motor function and sensory alteration has been slower, since it depends upon a gradual recovery of the damaged nerve roots.

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UTERINE CANCER: ROENTGEN RAY THERAPY*

By DANIEL G. MORTON, M.D.
San Francisco

DURING the past ten years high voltage roentgen radiation has become a standard supplement to the radium treatment of uterine cancer. The voltages most generally used have been in the neighborhood of 200,000. Within the past few years, machines developing even higher potentials have become available in a few institutions. The supervoltages employed with these machines have ranged around 800,000. Opinions regarding the efficacy of roentgen therapy have varied, but most observers have felt that the results of radium ir-

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radiation were being improved. The 200 kv. radiations have now been in use long enough to allow some analysis of the results, while 800 kv. radiations still remain in the experimental stage. The present investigation is an attempt to evaluate the results of roentgen therapy obtained at the University of California Hospital in the treatment of cervical cancer. It is a source of great regret that the number of cases is small, for this makes definite conclusions impossible. However, it is felt that tendencies can be detected even in the results of a small series.

CLINICAL MATERIAL UNDER OBSERVATION

The material surveyed in this study consists of one hundred cases treated between April 1, 1931, when roentgen irradiation with 200 kv. was first started as a supplement to radium therapy for cervical cancer, and March 31, 1936. Thirty-two patients were treated more than five years ago, 58 more than four years ago, 82 more than three years ago, and 100 more than two years ago. In an additional sixteen cases, roentgen radiation was carried out for recurrences. Thirteen patients received two full courses.

TABLE 1.—*Material*

Roentgen radiation—primarily	100 cases
32—Five-year cases	82—Three-year cases
58 —Four-year cases	100—Two-year cases

An additional twenty-nine courses were given during this period, sixteen for recurrences, thirteen were second courses.

Supervoltage has been used in a number of the cases for the past four years. In reporting the results no distinction is made with reference to voltage, as the experience with supervoltage is not extensive enough to permit separate consideration. Only those cases are included in which full courses were given shortly before, at the time of, or shortly after the application of radium. This means the exclusion of a number of patients who were treated for recurrence a year or two after their primary radium treatment and a number who received incomplete courses. Also excluded are all cases in which operation was employed. The plan of treatment at this institution is to treat surgically all early cases (Groups 1 and 2), provided age and general condition do not contraindicate the radical operation; the remainder are treated radiologically. Thus we have had a total of 354 five-year cases between 1916 and March 31, 1933. Twenty-eight per cent of the cases were classed as operable and 72 per cent as inoperable. Of the ninety-nine operable cases almost half were treated surgically. This means that the cases with the most advanced growths were reserved for radiation. This policy has been continued whether radium alone was used or radium and x-ray. Slightly more than one-fifth of all the patients have lived for more than five years after treatment, while only 16.9 per cent of those (the worst) treated radiologically have survived the five-year period. This information will serve as a background for the results to be reported.

TABLE 2.—*Type of Material Seen in This Clinic (Schmitz Classification)*

Group	Cases	
I II	35 64	Operable cases: Ninety-nine, or 28 per cent. Forty-eight of these were operated upon.
III IV	160 95	Inoperable cases: Two hundred and fifty-five, or 72 per cent.

Absolute five-year survival—22.9 per cent.
Absolute five-year survival, radiated cases only—16.9 per cent.

TECHNIQUE OF RADIATION

The technique of radiation which we employ is as follows: when the patient is first admitted a biopsy is taken and radon applied according to the Memorial Hospital method. This involves the use of 100 to 150 millicuries, equally distributed between three or four capsules. The aim is to give a total of 4500 mch.—2000 mch. in the cervical canal proper, 1000 mch. in the fundus, and 1500 mch. against the cervix. This may be supplemented according to circumstances. Often tubes are placed in the lateral vaginal fornices, or needles are inserted into the paracervical tissues. In some instances the patient receives as much as 7000 to 8000 mch. Usually the desired dose is arrived at in three sittings, a week apart. For the intracervical and intra-uterine applications the screening is Au 0.5 mm. and Rubber 2 mm. A tandem of three radon capsules in rubber tubing is used. For the vaginal applications, the screening is Au 0.5 mm., Br. 2.0 mm., Al 1.0 mm. Various plaques, boxes, and tubes are used. Constitutional reactions are rare, as are local burns. Fistulae, which could not be directly attributed to the advance of cancer, have not been observed with this method.

Roentgen therapy has been given before the radium in some cases, in which event a ten to thirty-day interval has been allowed between the termination of the x-radiation and the radium. In other cases the radium and x-ray have been given concurrently. For the past few years the radium has been given first, and followed in ten to twenty days by the roentgen therapy. This analysis has not shown one method to be more advantageous than the others. The roentgen therapy has been under the direction of Dr. Robert S. Stone. The 200 kv. radiations have come from a General Electric X-P tube activated by a constant potential apparatus at 200 kv. and 15 ma., and filtered through the wall of the tube (0.2 mm. Cu. equivalent) and 0.2 mm. Sn., 0.25 mm. Cu. and 2 mm. Al., or 0.5 mm. Cu. plus 1 mm. Al. Supervoltage radiations have come from the Sloan high-frequency generator, operated at from 600 to 1200 kv. and filtered through the tube wall of 1.5 mm. Cu. plus 3 mm. steel, and then through 2 mm. Pb., 1 mm. Cu., and 1.5 mm. Al. For further technical details I shall refer anyone interested to a recent publication by Doctor Stone,[1] in which the various physical factors are given. In general, four 10 by 20 centimeters fields—two anterior and two posterior—have been used. The number of roentgens per field has been gradually increased from 1000 to 1600 to the present dose of 2400 to 3000. No patient considered in this analysis received less than 1000 roentgens per field. The patients have been treated daily except Sundays for ten to thirty days. There have been, naturally, other minor changes in technique from time to time.

RESULTS

In Table 3 are given the results for the thirty-two five-year cases in which both radium and roentgen therapy were used. These are compared with the results obtained in all cases radiated, and with a group of cases radiated with radium alone between the years 1928 and 1931. This latter group is a better control group than all cases radiated because it contains about the same proportion of operable and inoperable cases, and because the radium technique employed during this time was

TABLE 3.—*Five-year Results*

Group	Radium and X-ray 1931-1933 Cases	Survival	Radium Alone 1928-1931 Cases	Survival	All Cases Radiated 1916-1933 Cases	Survival
I	1	1 or 100 per cent	6	4 or 66.7 per cent	17	13 or 76.5 per cent
II	5	2 or 40 per cent	8	2 or 25 per cent	34	12 or 35.3 per cent
III	15	5 or 33.3 per cent	38	6 or 15.8 per cent	156	24 or 15.4 per cent
IV	11	1 or 9.1 per cent	27	None	95	2 or 2.1 per cent
Total	32	9 or 28.1 per cent	79	12 or 15.2 per cent	302	51 or 16.9 per cent
	18.8 per cent operable		17.7 per cent operable		13.5 per cent operable	
	81.2 per cent inoperable		82.3 per cent inoperable		86.5 per cent inoperable	

roughly similar to that used in conjunction with roentgen therapy. The 28.1 per cent five-year survival obtained for the group treated with roentgen rays is almost twice as great as the percentage of survivals after radium alone. This difference is illustrated more graphically by the survival curves for these two groups, shown in Figure 1.

Curves have also been constructed for the four, three and two-year cases (Figures 2, 3, and 4, respectively). This has been done because of the small number of five-year cases available. While it is realized that no great stock should be put in results obtained in less than five years, we believe that such results can at least indicate trends. The same control group is retained in each comparison. These curves indicate that much better results have been obtained after four, three, and two years following radium and roentgen therapy than were obtained at the same periods following radium alone. It is interesting that such marked improvement continues even in the face of a constantly increasing proportion of advanced growths among the cases treated since roentgen therapy was started. This change in the quality of the material is graphically illustrated in Figure 5.

The improvement in results must be explained upon the presumption that roentgen rays generated at high voltages are capable of reaching and killing cancer cells in portions of the pelvis which are inaccessible to the gamma rays of radium as ordinarily applied. Certainly, we are aware that cancer is present in the regional glands of a large proportion of Groups 3 and 4 cases. We are equally cognizant that cancer in these locations cannot be affected materially by radium in the cervix or vagina. Therefore, we cannot expect to cure patients with regional gland involvement with radium alone. Presumably, roentgen radiation may destroy the cancer existing in regional glands, and thus account for the better results obtained in cases so treated. For several years we have been removing the regional glands in certain borderline cases. Some have received roentgen radiation and others have not. In time it should be possible to demonstrate a difference in the percentage of cases with involved glands, if roentgen radiation does in fact destroy cancer in these locations.

Of considerable interest is the recent report of Schmitz.[2] Of thirty-four cases of cervical cancer treated by 800 kv. radiations alone, no radium, seventeen, or 50 per cent, were alive and well at the end of three years. While this is only a three-year result, it indicates marked improvement over the results of the older methods. Schmitz believes that 800 kv. radiations are much more efficacious than 200 kv. radiations. Whether he is correct in this or not, his results point definitely to the relative effectiveness of high voltage radiation for cervical cancer.

REACTIONS

One of the principal disadvantages of high-voltage radiation is the immediate reaction. In treating cervical cancer it is necessary to expose comparatively large areas of the lower abdomen to the rays, consequently numerous loops of bowel, the bladder, and the rectum are subjected to large amounts of radiation. This often results in making

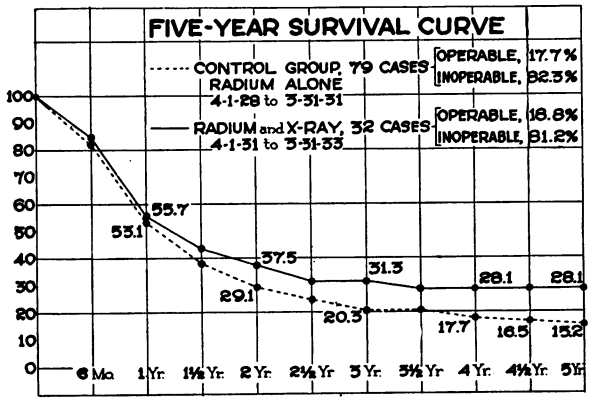

Fig. 1

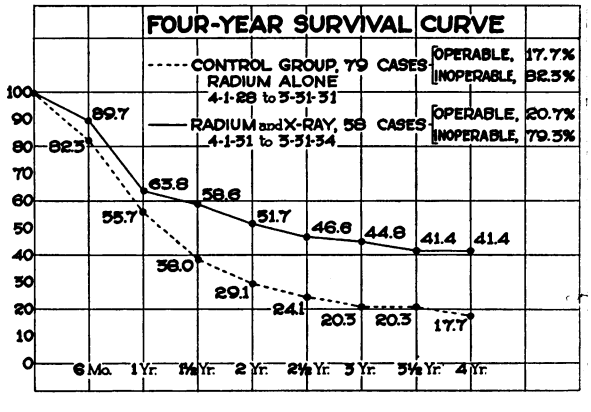

Fig. 2

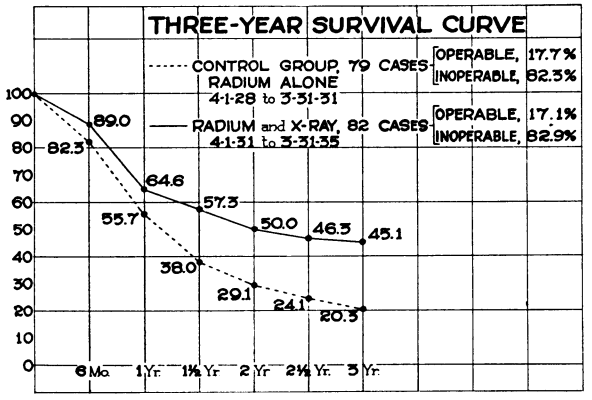

Fig. 3

the patient sick and miserable. The usual symptoms are nausea, vomiting, anorexia, loss of weight, diarrhea, urinary frequency, and tenesmus. Blood counts during the course of therapy show a leukopenia and relative lymphocytosis, and anemia, which generally are quite transient. The severity of the symptoms varies with the individual and with a number of physical factors discussed below. These reactions are of great importance because they sometimes result in the death of the patient or interruption of treatment. Some designate nausea and vomiting and the blood-changes as constitutional reactions. The explanation for such reactions is unknown. The remainder of the symptoms are mostly due to the irritation and destruction of the mucosa of the bowel and bladder. Some degree of this type of reaction is unavoidable. Physical factors which may influence the severity of the immediate reactions are kilovoltage, the total dose, the daily rate at which the radiations are given, the total duration of the treatments, the number and size of the fields, the number of fields treated at a time (and thus the volume of tissue radiated), etc. Indeed the large number of variable factors makes it almost impossible to correlate the individual variations in reactivity with any particular factor.

During the period under consideration, 129 courses of roentgen therapy were given to 116 patients with cervical cancer. I have attempted to evaluate reactions, dividing them into mild, moderate, and severe. No attempt has been made to separate so-called constitutional symptoms from those

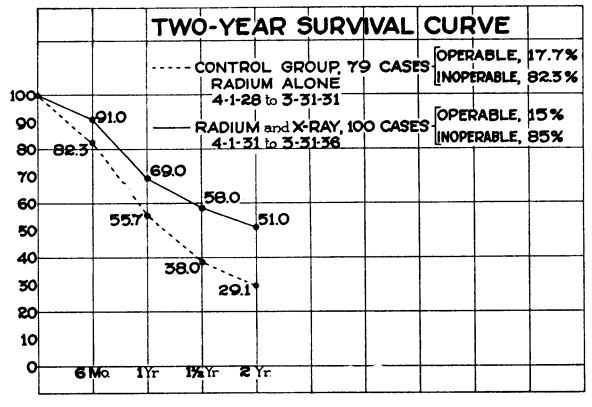

Fig. 4

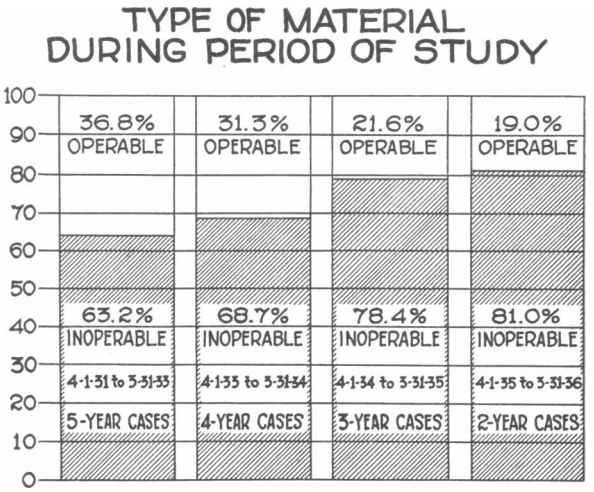

Fig. 5

due to mucosal destruction. The reaction was considered severe when there were marked nausea and vomiting, frequent and distressing diarrhea, marked loss of weight, and the patient was so sick that she was able to continue the treatments with difficulty. Hospitalization was required for many of these patients, and some of them died. The reaction was considered mild when nausea was slight or absent, diarrhea was mild and easily controlled, and anorexia and weight loss were minimal. Included under this heading are a number of cases in which little or no comment regarding the reaction was made at the time, presuming that a severe reaction would have provoked comment. The reactions were classified as moderate when the symptoms were quite marked, but caused no serious disability on the part of the patient. The results are tabulated in Table 4.

TABLE 4.—*Immediate Reactions to Roentgen Radiation*

Anorexia, Nausea and Vomiting, Diarrhea, Loss of Weight, Leucopenia, Anemia	
Mild reactions	77 or 59.6 per cent
Moderate reactions	28 or 21.7 per cent
Severe reactions	24 or 18.7 per cent
Total	129*

* Total patients 116; thirteen had two courses.

Slightly less than one-fifth of the patients experienced severe reactions. The remainder were either moderately or only mildly upset.

In Table 5 the cases are divided according to whether treatment consisted of 200 kv. or 800 kv. radiations.

TABLE 5.—*Type of Reaction Correlated With Kilovoltage*

	200 Kv. Cases	89 Cases Per Cent	800 Kv. Cases	40 Cases Per Cent
Mild	59	66.2	18	45
Moderate	20	22.4	8	20
Severe	10	11.4	14	35

Severe reactions were encountered in 35 per cent of the latter, as compared with 11.4 per cent of those treated with 200 kv. radiations. To put it another way, fourteen, or more than one-half of the entire number of the severe reactions, occurred after supervoltage radiations, which were used in less than one-third of the courses given. This does not necessarily mean that supervoltage *per se* was responsible, as there are other variables to be considered. Much larger daily and total doses were given with the 800 kv. machine than with the 200 kv. Thus, the increased number of roentgens given with the supervoltage machine may have been responsible for the greater proportion of severe reactions following its use. For instance, nine of the fourteen severe reactions with supervoltage occurred in cases receiving more than 3000 r per field. I have not attempted to correlate the type of reaction with the physical factors in further detail because of the many variables.

Regarding the skin reactions, satisfactory healing has taken place eventually with few exceptions. Doctor Stone,[1] to whose publication I shall refer you for more detailed consideration of skin reactions, believes that increases in dosage are limited by the mucosal changes more than by the skin changes. As with the mucosal reactions, the more severe skin reactions have followed the higher daily and total doses per port. In a number of patients the end-result has been the production of a thick, fibrous, or "leather" skin. Sometimes the skin is so inelastic, and stretched over the sacrum, that some difficulty is experienced in bending over.

Other unpleasant late effects have developed after roentgen radiation. In three cases in this series, intestinal obstruction, which seemed to be independent of the spread of cancer, has occurred. It is our impression that this is much more likely to occur in patients who have had a previous laparotomy. Often in such patients there are fixed loops of bowel which, in the course of x-radiation, receive more than their share. As a matter of fact, all of the patients developing this complication had had a previous abdominal operation. This complication has also been observed in a few cases not in this series.

There have been three cases in which serious bone changes developed. In one, discovered only at autopsy, there was marked destruction of the symphysis without carcinomatous invasion. In two cases fracture of the neck of the femur occurred, without roentgenologic evidence of metastasis. The amount of radiation employed in these cases was not greater nor was the technique different in any way from the usual. Whether these bone changes were due to a direct destructive effect of the roentgen rays, or were secondary to obliterative vascular changes, is a matter of conjecture.

Six patients died as a consequence of radiation. (Table 6.) These deaths can hardly be attributed to the direct effect of roentgen rays, except perhaps the one in which no cause for death could be found at autopsy except such extreme destruction of the tumor that cancer cells could no longer be definitely identified. In the remainder, however, sufficiently significant changes were set up to cause the patients' deaths within a few days to a month. No death has been included in which there was any suggestion that the advance of cancer alone might have been the responsible factor. Several other deaths, not included, possibly were hastened by the radiation.

TABLE 6.—*Mortality*

There were six deaths associated either directly or indirectly with the roentgen therapy	
1. Peritonitis	1,000 kv. machine—3,476 r.
2. Heart disease, general prostration	1,000 kv. machine—3,160 r.
3. Marked degeneration of tumor	200 kv. machine—1,800 r.
4. Hemorrhage	200 kv. machine—1,500 r.
5. Urinary infection	200 kv. machine—1,700 r.
6. Intestinal obstruction	200 kv. machine—1,500 r.

Radium may have played a part in causing some of these deaths. However, two patients were not treated with radium and three others received small doses only. Placing the responsibility for the mortality upon either of the agents is of little moment. The important fact to realize is that the radiation treatment of cervical cancer carries a mortality in the neighborhood of 5 per cent.

SUMMARY

To summarize: One hundred cases of cervical cancer in which high-voltage roentgen radiation was employed as a part of the treatment have been analyzed. Only thirty-two of these patients were treated more than five years ago. The early results indicate improvement over those obtained with radium alone. While we believe that we may infer that roentgen radiation is a valuable part of the treatment of cervical cancer, the small number of cases does not permit definite conclusions. Severe immediate reactions to roentgen radiation occurred in about one-fifth of the cases. The majority of these followed supervoltage radiation and occurred when more than 3000 r per field was given. There were six deaths associated either directly or indirectly with roentgen therapy.

CONCLUSIONS

1. High-voltage roentgen radiation is of value in the treatment of cervical cancer.

2. Roentgen therapy carries a morbidity and mortality.*

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* **Addenda.**—Since this article was written, another year has passed, so that now there are fifty-eight patients treated five or more years ago. The survival rate is 39.5 per cent, a continued improvement showing up in a larger number of patients.